# WHAT MAKES TGC PROTOCOLS "T" (TIGHT)? AN ANALYSIS OF DATA FROM 2 STUDIES

M.S. Fatanah, A. Le Compte, J. C. Preiser, P. Massion, R. Rademecker, C.G. Pretty, G.M. Shaw, J. Lin, T. Desaive, J.G. Chase

## INTRODUCTION

Critically ill patients experience stress induced hyperglycemia and high levels of insulin resistance. The occurrence of hyperglycemia, particularly severe hyperglycemia is associated with increased morbidity and mortality. However, any tight glycemic control (TGC) result has to be viewed in the context of:

- Patient condition and cohort
- Levels and dosing of insulin and nutrition relative to glycemic levels (i.e. the protocol)
- Adoptability of the protocol to acute changes in patient condition.

The goal is to uncover aspects of successful tight glycemic control and delineate any differences in cohort that might require a less general, hospital/region specific approach to tight glycemic control.

## MODELS

Insulin sensitivity was fitted to retrospective data from glucose control under each protocol (SPRINT and Glucontrol). Model-based insulin sensitivity provides a measure of overall patient response to exogenous insulin and can indicate level of glycemic response and overall clinical condition.

Stochastic modelling is used to construct distributions from the model-identified insulin sensitivity ($S_I(t)$) profiles, which define the variability in $S_I$ and thus patient condition for each house of glucose control.

$$\dot{G} = -p_G G - S_I G \frac{Q}{1+\alpha_G Q} + \frac{P(t) + EGP_{max} - CNS}{V_G(t)}$$

$$\dot{Q} = kQ + kI$$

$$\dot{I} = -\frac{nI}{1+\alpha_I I} + \frac{u_{ex}(t)}{V_I} + e^{-k_I U_{ex}(t)} I_B$$

## METHODS

Comparisons of glycemic control with published studies often rely on comparing summary data presented in literature. The Glucontrol and SPRINT studies represent two completely independently designed and implemented protocols. Clinical data and model-based information from both studies are compared.

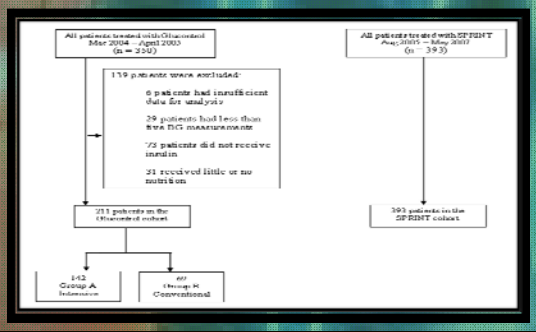
### Glucontrol

- Leige, Belgium
- 350 patients
- Requires current and previous BG and prior insulin bolus size.
- 1-4 hour BG measurement interval
- Insulin delivered via infusion
- BG targets:
  - Intensive Group (A):
    - 4.4 to 6.1 mmol/L
  - Conventional Group (B):
    - 7.8 to 10 mmol/L

### SPRINT

- Christchurch, New Zealand
- 393 patients
- Uses current and previous BG, current feed rate and prior insulin bolus size.
- 1-2 hour BG measurement interval
- Insulin delivered via bolus, maximum of 6U/hr
- BG target: 4.4 to 6.1 mmol/L

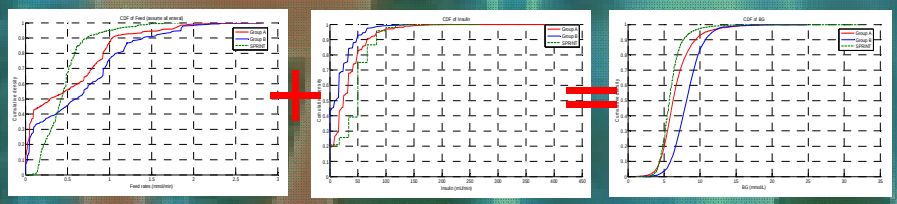
### COHORT SELECTION




## RESULTS AND DISCUSSION

Comparison of Glucontrol and SPRINT cohorts

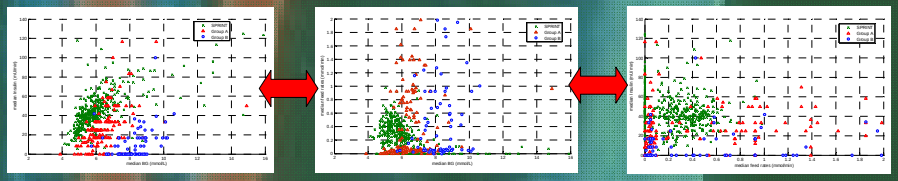
| | Glucontrol | | SPRINT |
|---|---|---|---|
| | A | B | |
| Number of patients | 142 | 69 | 393 |
| Male (%) | 64.8 | 56.5 | 62.8 |
| Apache II score median [IQR] | 17 [14 - 22] | 17 [14 - 21] | 18 [14 - 24] |
| Hours of control | 16,831 | 12,946 | 49,008 |
| Total BG measurements | 4,571 | 2,820 | 29,919 |
| BG median [IQR] (mmol/L) | 6.5 [5.3 - 7.6] | 8.2 [6.9 - 9.4] | 5.7 [5.0 - 6.6] |
| Insulin rate median [IQR] (mU/min) | 25.0 [8.3 - 50.0] | 11.7 [0.0 - 28.3] | 50.0 [16.7 - 50.0] |
| Feed rate median [IQR] (mmol/min) | 0.30 [0.00 - 0.90] | 0.60 [0.10 - 1.00] | 0.42 [0.25 - 0.52] |
| Percentage of measurement less than 2.2 mmol/L (%) | 0.40 | 0.10 | 0.05 |
| Percentage of measurement less than 4.4 mmol/L (%) | 9.4 | 1.7 | 9.4 |
| Percentage of measurement between 4.4 and 6.1 mmol/L (%) | 35.8 | 10.4 | 48.2 |



✓SPRINT achieved tighter BG (steeper CDF).

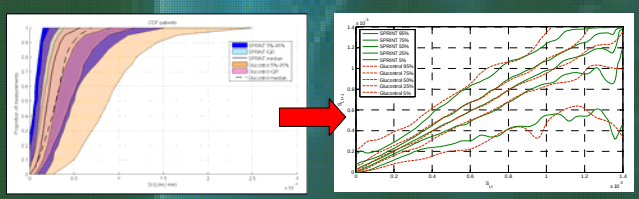
✓SPRINT provided nutrition more regularly and slightly higher insulin infusion rates in compensation

✓SPRINT provided a more constant nutrition rate to balance the insulin given with for less variation than the Glucontrol case where nutrition rate is not a controlled variable.



✓SPRINT used tighter, more consistent insulin and nutrition (CHO all sources) inputs. The balance of insulin and nutrition was more balanced (less variable)

✓Glucontrol used wide ranges of insulin and nutrition that were not well balanced clinically. The result was more variable BG outcomes in control



- The Glucontrol cohort had higher insulin sensitivity at all likelihoods and for all observed percentiles compared to the SPRINT cohort.

- Stochastic modelling shows similar distributions of variability in $S_I$.
- ***So, $S_I$ is different but evolves similarly over time. Patient variability is a constant?***

- ***The Moral***: All things in moderation and balance
- ***The Technical Moral***: You must know your nutrition to minimise the outcome BG variability (and patient variation)
- ***An Idea***: *Is unknown, variable nutrition protocols a cause of variable outcomes in multicentre trials?*

Canterbury District Health Board
Te Poari Hauora o Waitaha

UC BIOMEDICAL ENGINEERING

UC UNIVERSITY OF CANTERBURY